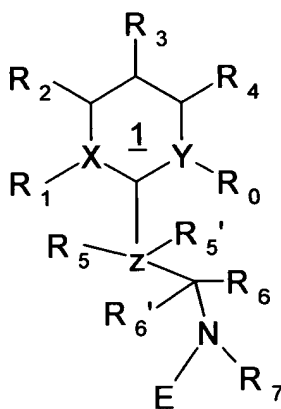


WE CLAIM:

1. A hydrophilic transportable dopaminergic prodrug compound according to FORMULA V,



Formula V

wherein,

Ring 1 comprises an aryl or heteroaryl ring having 4 to 8 carbon atoms, among which atoms are counted "X" and "Y";

each of X and Y is optional; X, when present is either -C(R₁)₂- or -C(R₁)₂-; Y, when present, is either -CH₂- or -CH₂-CH₂-;

z, R₅ and R_{5'} are optional, and when present z, R₅ and R_{5'} together form a lower alkyl or a substituted lower alkyl moiety;

N is part of either an amine or an amide linkage;

E is a saccharide which forms a linkage with N through a single bond from a carbon or oxygen atom thereof;

R₁ and R₄ are selected from the group consisting of hydrogen, hydroxyl, halogen, halo-lower alkyl, alkoxyl, alkoxyl-lower alkyl, halo-alkoxy, thioamido, amidosulfonyl, alkoxycarbonyl, carboxamide, aminocarbonyl, and alkylamino-carbonyl;

R₂ and R₃ are hydroxyl;

R₅ and R₆, when present, are selected from the group consisting of hydrogen, hydroxyl, alkoxyl, carbonyl, alkoxycarbonyl, aminocarbonyl, alkylamino-carbonyl and dialkylamino-carbonyl; and,

R₆ and R_{6'} are selected from the group consisting of hydrogen, hydroxyl, alkoxyl, carboxyl, alkoxycarbonyl, aminocarbonyl, alkylamino-carbonyl and dialkylamino-carbonyl,

with the proviso that Ring 1 is capable of binding to any of:

a dopaminergic receptor selected from the group consisting of a D1 receptor and a D5 receptor; a DAT transporter; a VMAT transporter; and,

with the proviso that E is capable of binding to a GLUT transporter selected from the group consisting of a GLUT1 receptor and a GLUT3 receptor.

2. The prodrug compound of claim 1, wherein the E substituent is selected from the group consisting of a radical of a monosaccharide, a disaccharide, a trisaccharide and an oligosaccharide

3. The prodrug compound of claim 1, wherein the E monosaccharide comprises a radical of a sugar selected from the group consisting of aldose, ketoaldose, alditols, ketoses, aldonic acids, ketoaldonic acids, aldaric acids, ketoaldaric acids, amino sugars, keto-amino sugars, uronic acids, ketouronic acids, lactones and keto-lactones.

4. The prodrug compound of claim 3, wherein said radical of a sugar is further selected from the group consisting of triosyl, tetraosyl, pentosyl, hexosyl, heptosyl, octosyl and nonosyl radicals and derivatives thereof.

5. The prodrug compound of claim 4, wherein said pentosyl sugar radical comprises a straight carbon chain, a furanosyl ring or a derivative thereof.

6. The prodrug compound of claim 4, wherein said hexosyl sugar radical comprises a straight carbon chain, a furanosyl ring, a pyranosyl ring or a derivative thereof.

7. The prodrug compound of claim 4, wherein said hexosyl radical is further selected from the group consisting of allose, altrose, glucose, mannose, gulose, idose, galactose, talose, fructose, ribo-hexulose, arabino-hexulose, lyxo-hexulose and derivatives thereof.

8. The prodrug compound of claim 4, wherein said pentosyl radical is further selected from the group consisting of ribose, arabinose, xylose, lyxose, ribulose, xylulose and derivatives thereof.

9. The prodrug compound of claim 4, wherein said heptosyl residue comprises sedoheptulose and derivatives thereof.

10. The prodrug compound of claim 4, wherein said nonosyl residue comprises N-acetylneuraminic acid, N-glycolylneuraminic acid, diacetylneuraminic acid, and derivatives thereof.

11. The prodrug compound of claim 7, further comprising glucose, galactose, fructose or derivatives thereof.

12. The prodrug compound of claim 2, wherein said disaccharide, trisaccharide and oligosaccharide comprise a sugar homopolymer or a sugar heteropolymer.

13. The prodrug compound of claim 2, wherein said sugar homopolymer comprises a glycoside selected from the group consisting of erythran, threan, riban, arabinan, xylan, lyxan, allan, altran, glucan, mannan, gulan, idan, glalactan, talan, fructan and derivatives thereof.

14. The prodrug compound of claim 2, wherein said sugar heteropolymer further comprises a glycoside selected from the group consisting of erythroside, threoside, riboside, arabinoside, xyloside, lyxoside, alloside, altroside, glucoside, mannoside, guloside, idoside, galactoside, taloside, fructoside and derivatives thereof.

15. The prodrug compound of claim 3, wherein said glycoside further comprises a riban, an arabinan, a glucan, a galactan, a mannan and derivatives thereof.

16. The prodrug compound of claim 4, wherein said glycoside further comprises a riboside, an arabinoside, a glucoside, a galactoside, a mannoside, a fructoside and derivatives thereof.

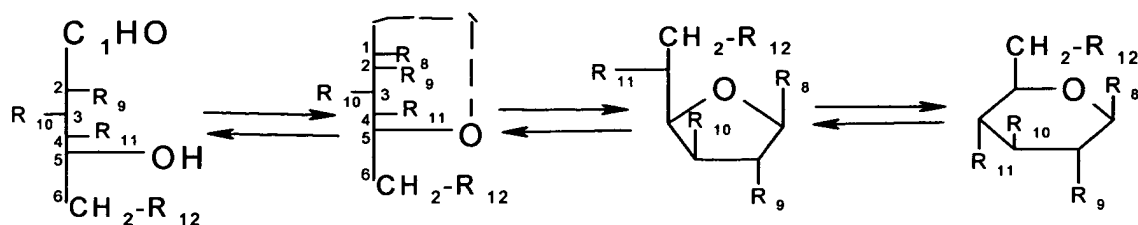
17. The prodrug compound of claim 15, wherein said glucan comprises maltose, amylose, glycogen, cellobiose, amylopectin, heparin and derivatives thereof.

18. The prodrug compound of claim 16, wherein said glucoside comprises sucrose and derivatives thereof.

19. The prodrug compound of claim 16, wherein said fructoside comprises fucosidolactose and derivatives thereof.

20. The prodrug compound of claim 16, wherein said galactoside comprises lactose, hyaluronic acid, pectin and derivatives thereof.

21. The prodrug compound of claim 7, further comprising a sugar according to FORMULAS VIa, VIb, VIc and VIId,



Formula VIa

Formula VIb

Formula VIc

Formula VIId

wherein, R₈, R₉, R₁₀, R₁₁ and R₁₂ are selected from the group consisting of hydroxyl, hydrogen, methyl, halogen, lower alkyl, halo-lower alkyl, alkoxy, ketone, carboxyl, amine, amido, N-acetyl, N-methyl, N-linked lower alkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, phosphate, sulfate and thiol.

22. The prodrug compound of claim 1, further comprising a compound that binds to dopamine receptor in a mammalian cell.

23. The prodrug compound of claim 1, further comprising a compound that bind to and is transportable by a DAT transporter in a neural cell.

24. The prodrug compound of claim 1, further comprising a compound that binds to and is transportable by a GLUT transporter in a neural cell or a vascular endothelial cell.

25. The prodrug compound of claim 1, further comprising a compound transportable at the blood brain barrier by an endothelial cell.

26. A dopaminergic pharmaceutical composition comprising: one or more of an additive, a stabilizer, a carrier, a binder, a buffer, an excipient, a filler, an emollient, a disintegrant, a lubricating agent, and antimicrobial agent; and, a hydrophilic transportable dopaminergic prodrug compound according to claim 1.

27. The dopaminergic pharmaceutical composition of claim 26, further comprising a form suitable for dermal administration, oral administration, buccal administration, trouch administration, perenteral administration, injection, intra-rectal administration, intrathecal administration, intra-nasal administration, intra-bronchial administration and intra-ocular administration.

28. The dopaminergic pharmaceutical composition of claim 27, wherein said form is selected from the group consisting of a syrup, an elixir, a tablet, a lozenger, a capsule, a perenteral solution, an injection solution, an nasal solution, an eye drops solution, a powder, a granule, a timed-release capsule, an emollient cream, a salve, an ointment, an impregnated bandage, a timed-release lipid soluble patch, a trouch and a suppository.

29. A method for preparing a pharmaceutical composition comprising the step of adding one or more of additives, a stabilizers, carriers, binders, buffers, excipients, fillers, emollients, disintegrants, lubricating agents, or antimicrobial agents to a hydrophilic transportable dopaminergic prodrug compound according to claim 1.

30. A hydrophilic prodrug dopaminergic pharmaceutical composition for metabolic replacement therapy in a subject with Parkinson's disease or a Parkinson's related disease comprising a compound according to FORMULA I,

A-B-D-E

Formula I

wherein,

A, comprises a cyclic, heterocyclic, aryl or heteroaryl ring capable of binding to both a dopamine receptor and a dopamine transporter in a neural cell; B, comprises a bridging lower alkyl moiety linked through single bonds with each of A and D; D, comprises an amide or an amine linked through single bonds with each of B and E; E, comprises a saccharide moiety; and,

said compound according to FORMULA I binds to and is transportable by a GLUT in a blood cell; binds to and is transportable by a GLUT in a vascular endothelial cell; binds to and is transportable by a DAT; and is capable of binding to a dopamine receptor in a neural cell.

31. A method for treating a dopaminergic transcription regulatory defect in a subject in need thereof, comprising the step of administering to the subject a compound

effective to bind and activate both a GLUT and a DAT in a neural cell, wherein the activation of the GLUT or the DAT is effective to alter the transcription of a dopaminergic gene in the neural cell, wherein the dopaminergic gene is selected from the group consisting of a tyrosine hydroxylase gene, an aromatic decarboxylase gene, a monoamine oxidase gene, a DAT gene, a VMAT2 gene, a Nurr1 or a Nurr2 gene, an SP1 or SP3 gene, a dopaminergic receptor gene, a synuclein gene, an Elk gene, a Hic-5 gene, an Lmx1b gene, a Pitx3 gene, a HoxA5 gene, a HNF-3 β gene and a HoxA4 gene.

32. A method for identifying a candidate drug substance for treating a dopaminergic transcription regulatory defect, comprising the steps of:

measuring binding or transport of a test compound by a GLUT or by a DAT transporter;

measuring transcription of a dopaminergic gene selected from the group consisting of a tyrosine hydroxylase gene, an aromatic decarboxylase gene, a monoamine oxidase gene, a DAT gene, a VMAT2 gene, a Nurr1 or a Nurr2 gene, an SP1 or SP3 gene, a dopaminergic receptor gene, a synuclein gene, an Elk gene, a Hic-5 gene, an Lmx1b gene, a Pitx3 gene, a HoxA5 gene, a HNF-3 β gene and a HoxA4 gene;

determining that the test compound is the candidate drug substance if the test compound is bound or transported by either of the GLUT or the DAT transporters and that the transcription of the dopaminergic gene is increased or decreased relative to a vehicle treated negative control.

33. The method of claim 32, wherein the test compound is transported by a GLUT3 transporter.

34. The method of claim 32, wherein the test compound increases the transcription of a tyrosine hydroxylase gene.

35. The method of claim 32, wherein the test compound decreases the transcription of an alpha-synuclein gene.

36. The method of claim 32, wherein the test compound increases the transcription of a Nurr gene.

37. The method of claim 36, wherein the increased mRNA transcript of the Nurr1 gene is Nurr1 or Nurr2.

38. A method for treating a tyrosine hydroxylase genetic defect in a subject in need thereof, comprising the step of administering to the subject a pharmaceutical compound transportable by both a GLUT-3 transporter and DAT transporter in a manner effective to increase transcription of the tyrosine hydroxylase gene in the subject.